Urologic Oncology: Extraordinary Opportunities for Discovery

Highlights from the 2nd Annual Winter Meeting of the Society of Urologic Oncology December 1–2, 2001, Bethesda, MD

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The 2nd Annual Winter Meeting of the Society of Urologic Oncology (SUO) was held in the Natcher Conference Center of the National Institutes of Health in Bethesda, Maryland on December 1–2, 2001. The SUO was created in 1984 to include members interested in the care of patients with malignant genitourinary disease. The SUO develops educational and research initiatives, one of which is this winter oncology meeting, which is jointly sponsored by the National Cancer Institute and the Society of Urologic Oncology. Physicians, scientists, fellows, and medical and urologic oncologists attended to listen to state-of-the-art lectures presented by experts from all over the United States and Canada.

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Furthermore, there was a poster session with 50 abstract presentations, many of which were presented by fellows in training, which was a forum for basic research. This meeting was designed to facilitate discussion of important issues among members of the urologic oncology community at the National Institutes of Health.

The meeting was broadly organized into three sessions devoted to the major urologic malignancies: transitional cell carcinoma (TCC), kidney cancer, and prostate cancer.

Transitional Cell Carcinoma

The first morning was devoted to the management of TCC of the bladder. This session was moderated by Dr. Richard Williams, Chairman of Urology at the University of Iowa, who also began the session with an overview of critical issues in noninvasive bladder cancer. According to Dr. Williams, superficial TCC is a heterogeneous disease with a variety of clinical behaviors. There are low-grade tumors, which tend to recur but pose little risk of progression to invasive disease. There are also higher-risk tumors, such as Grade 3 Ta, T1, and carcinoma in situ tumors that portend a greater risk of disease progression. However, there is still no reliable way to predict for the individual patient who will recur and who will progress. Dr. Williams stressed the urgent need for a validated tumor marker that can be used to determine who can be managed conservatively and who should be treated aggressively with early cystectomy.

These themes were expanded by Dr. H. Barton Grossman, of the University of Texas/MD Anderson Cancer Center, who discussed the current state of molecular markers of recurrence and progression. Although a number of molecular tests are available for TCC detection, there are

no validated tests for prediction of outcome or response to therapy. Dr. Grossman reviewed a number of promising technologies, including microsatellite analysis, fluorescence in situ hybridization, proteomics, as well as molecular markers such as P53 and Rb.

Dr. Harry Herr gave a clinical talk based on long-term follow-up of a cohort of patients he has followed at Memorial Sloan-Kettering Cancer Center, with advice regarding the optimal timing of cystectomies that suggested that early cystectomy may increase bladder cancer survival. He discussed the results for 307 patients with high-risk superficial TCC treated initially with transurethral resection. Of these, 90 patients eventually underwent cystectomy for tumor recurrence. With 15 years of follow-up analyzed, the survival for 48 patients treated with earlier cystectomy was 69%, whereas the survival of 42 patients who underwent cystectomy after 2 years of delay was only 26%. The same trend held true both for patients who recurred with superficial disease as well as muscle-invasive TCC.

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Kidney Cancer

The kidney cancer session was moderated by Dr. Jean deKernion, Chairman of Urology at the University of California, Los Angeles. Dr. Inderbir Gill spoke on the Cleveland Clinic experience with laparoscopic radical nephrectomy, and suggested that for many patients this was an oncologically satisfactory standard of care, which at least in his hands could be performed with similar operative time and blood loss as open nephrectomy, with shorter hospitalizations, quicker convalescence, and comparable cost of hospitalization.

Dr. Robert Flanigan, Chairman of Urology at Loyola University Medical Center, discussed the role of nephrectomy in metastatic kidney cancer and presented the final results of the Southwest Oncology Group study 8949, which randomized patients to nephrectomy followed by interferon versus interferon alone.[1] This phase III study showed a clear survival advantage to the patients who underwent initial cytoreductive nephrectomy across all stratifications that were analyzed. Median survival in the surgical arm was 12 months compared to 8 months in the immunotherapy-only arm, a difference that was statistically significant using a one-tailed analysis.

Two speakers from University of California, Los Angeles (UCLA) presented new data based on 10 years experience treating over 1000 patients in their multidisciplinary Kidney Cancer Program. Dr. Allan Pantuck presented a talk on the prognostic impact of retroperitoneal lymphadenopathy. The data from UCLA suggest that kidney cancer patients with regional lymph nodes, even those patients who have distant metastases, experience a decreased survival. Furthermore, survival of lymph node patients was the same regardless of treatment with immunotherapy, whereas node-negative patients had an improved survival when treated with postoperative immunotherapy. The median survival of patients with node-negative, metastatic disease treated with nephrectomy and postoperative immunotherapy was 28 months, compared to 12 months for metastatic patients with lymph nodes both with and without post-nephrectomy immunotherapy. Dr. Pantuck also presented data that suggested that for patients with both regional adenopathy as well as metastatic disease, survival was better in the patients who underwent retroperitoneal lymph node dissection as part of their care.

Dr. Amnon Zisman presented a new risk stratification system that is based on an extension of the UCLA Integrated Staging System for kidney cancer.[2] Decision boxes were presented that divide both nonmetastatic as well as metastatic patients into low, intermediate, and high-risk categories. Once a patient's risk classification has been determined, tables can be used to determine clinically relevant endpoints, such as survival, local recurrence, and response to immunotherapy. Interestingly, the survival of high-risk nonmetastatic patients was identical to the survival of low-risk metastatic patients, pointing to the urgent need for effective adjuvant strategies for high-risk localized patients.

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Prostate Cancer

Two sessions were devoted to prostate cancer, the first on basic science and novel therapies moderated by Dr. Christopher Logothetis of the

MD Anderson Cancer Center and the second on the management of high-risk/locally advanced disease moderated by Dr. Peter Scardino, Chairman of Urology at Memorial Sloan-Kettering Cancer Center. Dr. William Isaacs of the Johns Hopkins University School of Medicine discussed the ongoing search for a hereditary prostate cancer gene. Currently, at least 8 different genetic loci have been proposed. Dr. Isaacs focused on one gene, RNASE-L, located on the long arm of chromosome 1. This gene is involved in the induction of programmed cell death, and its loss leads to the accumulation of cells with damaged DNA. However, inactivating mutations of this gene have been found in only two families with familial prostate cancer so far. Dr. Martin Gleave from the University of British Columbia presented some new strategies for treating hormone-refractory prostate cancer, including the use of antisense targeting against progression-related genes, such as BCL-2 and clusterin. Dr. Neil Bander updated the results of ongoing clinical trials being performed at Cornell Medical Center in New York City, showing effective tumor targeting using antibodies targeting the prostate-specific membrane antigen in hormone-refractory patients.

Dr. Lawrence Klotz from the Sunnybrook Health Science Center in Toronto, Canada made a case for watchful waiting with select intervention for patients who progress, while Dr. S. Larry Goldenberg from the University of British Columbia discussed an ongoing, randomized study of 3 versus 8 months of neoadjuvant hormone therapy prior to radical prostatectomy.

Dr. Paul Lange and Dr. Paul Schellhammer, both Chairman of their respective urology programs at the University of Washington and the Eastern Virginia Medical School, presented the eligibility criteria and study design for a clinical trial that is now opening. The American College of Surgeons' Clinical Trials Group is initiating this important cooperative randomized trial (trial Z0070), which will compare surgery to radiotherapy for prostate cancer. This cooperative trial, which has been named SPIRIT (Surgical Prostatectomy vs Interstitial Radiation Intervention Trial), will eventually hopefully provide evidence that is currently lacking to compare these two common treatments for men with localized prostate cancer in terms of outcome and cancer specific survival. The trial will randomize low-risk prostate cancer patients to either radical prostatectomy or brachytherapy. Several thousand participants will be entered, and patients will be followed until a survival endpoint is reached. The difficulties of undertaking such a trial were discussed, and the attendees were exhorted to participate and to enroll patients into the study, as the relative efficacy of these two treatments can be compared only through the use of randomized, prospective clinical trials. ■

References

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2. Zisman A, Pantuck AJ, Dorey F, et al. Improved prognostication of renal cell carcinoma using an integrated staging system. *J Clin Oncol*. 2001;19:1649–1657.

Main Points

- Data from a Memorial Sloan-Kettering Cancer Center study suggest that early cystectomy may increase bladder cancer survival; of 90 patients who underwent cystectomy for tumor recurrence, after 15 years of follow-up the survival for 48 patients treated with earlier cystectomy was 69%, whereas the survival of 42 patients who underwent cystectomy after 2 years of delay was only 26%.
- A phase III study that randomized patients to nephrectomy followed by interferon or interferon alone showed a clear survival advantage to patients who underwent initial cytoreductive nephrectomy across all stratifications that were analyzed; median survival in the surgical arm was 12 months, compared to 8 months in the immunotherapy-only arm.
- Data from UCLA, based on the treatment of 1000 kidney cancer patients over a 10-year period, showed that the median survival of patients with node-negative, metastatic disease treated with nephrectomy and postoperative immunotherapy was 28 months, compared to 12 months for metastatic patients with lymph nodes both with and without post-nephrectomy immunotherapy.
- The American College of Surgeons' Clinical Trials Group is initiating an important study, the SPIRIT trial, which randomizes low-risk prostate cancer patients to either radical prostatectomy or brachytherapy. Several thousand participants will be entered, and patients will be followed until a survival endpoint is reached.